IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF PENNSYLVANIA

UNITED STATES OF AMERICA *ex rel.* **JOHN UNDERWOOD** **Plaintiff,** **v.** **GENENTECH, INC.** **Defendant.**	**CIVIL ACTION No. 03-3983**

SECOND AMENDED *QUI TAM* COMPLAINT

INTRODUCTION

1. This is an action to recover damages and civil penalties on behalf of the United States of America arising from fraudulent claims that defendant Genentech, Inc. ("Genentech") caused to be presented to the United States, in violation of the federal False Claims Act, 31 U.S.C. §§ 3729-32, as amended. These claims were fraudulent in that Genentech intentionally influenced medical care providers to present them by engaging in an illegal pattern of conduct, *i.e.*, off-label marketing of a pharmaceutical product and illegal kickbacks to physicians who prescribed that product.

2. Relator John Underwood is a citizen and resident of the state of Florida. From the start of the BioOncology franchise at Genentech in 1997, Mr. Underwood was a senior manager of sales development. From 2000 until 2003, he was a division sales manager to whom field sales representatives reported directly, and between 2003 and 2005, a senior hospital systems specialist. The facts averred herein are based upon Mr. Underwood's personal

observation, investigation, and documents in his possession, as well as Genentech's own business records.

3. Genentech is a biotechnology company incorporated in the state of California and rechartered in the state of Delaware. Genentech develops, manufactures, licenses and markets pharmaceutical products including prescription drugs falling under the jurisdiction and regulation of the United States Food and Drug Administration ("the FDA").

4. The federal government's Medicare program is a taxpayer-funded social insurance program that provides citizens 65 years of age and over with significant health insurance coverage. Medicaid is the United States health program for eligible individuals and families with low incomes and limited resources.

JURISDICTION AND VENUE

5. The Court has jurisdiction over the subject matter of this action pursuant to both 28 U.S.C. § 1331 and 31 U.S.C. § 3732, the latter of which specifically confers jurisdiction on this Court for actions brought pursuant to 31 U.S.C. § 3730.

6. This Court has jurisdiction over Genentech pursuant to 31 U.S.C. § 3732(a), which authorizes nationwide service of process, and because Genentech can be found and has transacted business in the Eastern District of Pennsylvania.

7. Venue is proper pursuant to 31 U.S.C. § 3732(a) in that Genentech can be found and has transacted business in the Eastern District of Pennsylvania.

8. Relator John Underwood has prepared and provided to the Attorney General of the United States and the United States Attorney for the Eastern District of Pennsylvania a disclosure pursuant to 31 U.S.C. § 3730(2) of material evidence and information in his possession related to this Complaint and of which he is the original source. This disclosure supports the validity of the claims presented herein.

BACKGROUND

9. The FDA is entrusted by law, 21 U.S.C. §§ 301 *et seq.*, with responsibility to ensure, among other things, that the American public is treated medically only with drugs that have been shown to meet certain standards with respect to efficacy and safety and that are appropriately labeled.

10. The FDA thus requires pharmaceutical companies to label their drugs with those use-indications, and only those use-indications, for which the drug has been shown, through extensive and rigorous clinical trials on animals and then on human beings, to be safe and to improve the medical condition of patients with those use-indications. Such use-indications are referred to as "on-label" indications.

11. The purpose of the law's requirement that pharmaceutical companies subject their drugs to sophisticated clinical trials is not only to protect the public from unsafe drugs, but also to prevent waste of public and private funds on ineffective drugs.

12. For a pharmaceutical company, the process of obtaining FDA approval of a drug for a particular use-indication or condition, and hence permission to include that use-indication on the drug's label, is long and extremely expensive. The law requires the company to

undertake this process, however, before the company can actually "market" the drug to health care providers and patients for that particular use-indication. 21 U.S.C §§ 331(d), 355.

13. By contrast, a health care provider is legally permitted to go beyond the "on-label" indications for a drug and prescribe it for a patient displaying different indications if, in his or her independent medical judgment, the patient requires that drug.

14. The incentives for a pharmaceutical company to break the law and market "off-label," that is, to try to persuade providers to prescribe the drug for non-approved indications, are considerable. The pharmaceutical company not only makes a profit, generally very substantial, from the sales of the drug for off-label uses, it also avoids having to pay for the years of expensive clinical trials required to get FDA approval of that indication for inclusion on the drug's label as an approved use.

15. Because off-label marketing is illegal, however, when pharmaceutical companies do it, they seldom do it in writing.

16. Defendant Genentech was well aware of the illegality of off-label marketing because, in May 1999 Genentech pled guilty to a federal criminal offense charging it with off-label marketing a growth hormone. The criminal information in that case charged that in off-label marketing this product, Genentech acted with intent to defraud the FDA. As a result of its guilty plea to that information, Genentech paid the federal government $50 million, $30 million of which was a criminal fine and $20 million of which was restitution to the government.

17. Despite its direct knowledge of the illegality of off-label marketing thus acquired, during the same period of time, 2000-2005, Genentech marketed a different drug, Rituxan, for off-label uses. It is Rituxan that is the subject of this lawsuit.

18. Rituxan can cause serious side effects, including:

(a) Progressive multifocal leukoencephalopathy (PML): This is a rare brain infection. PML usually causes death or severe disability. It mostly happens in patients with weakened immune systems, and can occur during treatment with Rituxan or after treatment has finished. There is no known treatment, prevention, or cure for PML; and

(b) Infusion reactions: Patients may get hives, swelling, dizziness, blurred vision, painful skin conditions, drowsiness, headache, cough, wheezing, or have trouble breathing while receiving or after receiving Rituxan.

19. In addition, patients on Rituxan “maintenance therapy”, as defined below, can develop significant immunodeficiency, delayed cytopenias, pulmonary toxicity and cardiotoxicity. Finally, maintenance Rituxan may lead to resistance to the drug in a patient’s body, a serious development that could make re-treatment upon relapse more difficult.

20. One of the principal uses of Genentech’s Rituxan is in the management of non-Hodgkins lymphoma (“NHL”). NHL is the fifth most common cancer in the United States; it is a disease that has stricken over 400,000 Americans, many of whom are covered by Medicare. Rituxan is also used for patients with chronic lymphocytic leukemia (“CLL”).

21. Genentech itself identified its target population for NHL alone as 300,000 patients.

22. During the period 2000-2005, Genentech knew that marketing was effective in persuading physicians to prescribe Rituxan, and aggressively marketed Rituxan to the physicians who were in a position to prescribe it for patients. In 2002, for example, Genentech's budget for marketing and sales of Rituxan exceeded $63 million, and in 2003 it exceeded $66 million. Genentech had approximately 100 sales representatives who called directly on the physicians across the United States; these calls occurred over 75,000 times every year. Genentech did not require its sales representatives to make or keep notes of the contents of any meetings with physicians or medical staff.

23. Genentech's total sales of Rituxan for the period encompassed by this Complaint rose sharply, from $262.7 million in 1999 to over $1.8 billion in 2005.

24. Between the beginning of 2000 and the end of 2005, the Medicare program paid Genentech well over $1.5 billion for Rituxan for senior citizens suffering from NHL. In 2003 alone, according to a Genentech document, the United States government, through its Medicare and Medicaid programs, paid out nearly $750 million to Genentech for Rituxan.

THE SCHEME

25. Unbeknownst to the Medicare and Medicaid programs, a significant portion of those enormous sums was the product of Genentech's illegal off-label marketing as set forth below.

26. The FDA first approved Rituxan in 1997 for the treatment of relapsed or refractory CD20+, B-cell low-grade non-Hodgkins lymphoma. In 2001 FDA also approved it

for retreatment of NHL patients who had relapsed, as well as for eight weekly doses ("infusions") per course of treatment and for treatment of NHL patients with "bulky" disease, a particular manifestation of NHL. All of these on-label indications are for NHL patients who are symptomatic.

27. There were no further FDA approvals for the use of Rituxan until 2006.

28. During the period 2000-2005, Genentech marketed Rituxan for the on-label uses just described, but the market for these on-label uses was becoming saturated.

29. Because of this limited market for Rituxan for on-label uses, Genentech devoted its substantial resources to marketing Rituxan off-label as well. In particular, Genentech marketed Rituxan (a) for so-called "maintenance" therapy (for patients who had completed an initial course of therapy and had become asymptomatic), alone or in combination with other drugs, in treating low-grade NHL and CLL; and (b) for both frontline therapy (for initial treatment of symptomatic patients) and maintenance therapy (for patients who had become asymptomatic) of patients with autoimmune diseases such as rheumatoid arthritis, idiopathic thrombocytopenic purpura, autoimmune hemolytic anemia, pure red cell aplasia and systemic lupus erythematosus.

30. At no time between 2000 and 2005 was Rituxan approved by the FDA for any use in asymptomatic patients, nor was it approved for autoimmune diseases, whether symptomatic or not.

31. In order to obscure the fact that it was marketing off-label for use in asymptomatic patients, Genentech sometimes called the use of Rituxan in such patients

"maintenance," sometimes "planned retreatment," sometimes "C & P" or "Compliance & Persistence," and sometimes "extended dosing."

32. In September 2003, for instance, Genentech conducted a national sales meeting in Colorado entitled "C & P Vision." The meeting focused on the profitability to Genentech of having patients treated with Rituxan as often as possible, *i.e.*, on the profitability of maintenance.

33. One of the first slides shown to Genentech sales personnel was entitled "Rituxan: Changing Sources of Growth," and it showed that "Maintenance" was the greatest source of growth in net revenue to Genentech from Rituxan: net revenue from maintenance was projected to grow by $311 million over the next three years, significantly more than net revenue from any other use for Rituxan was projected to grow. Another illustration broke this computation down, showing total "Maintenance Revenue" rising from $50 million in 2003, to $131 million in 2004, to $187 million in 2005, then to $361 million in 2006.

34. Sales personnel in that same national meeting were also shown a slide captioned "C & P SWOT Analysis," which listed under the heading of "Threats" to the growth of maintenance revenue, (a) the problem of "Reimbursement Barriers (Medicare reform…)", as well as (b) the problem of "Neutral results" of a scientific study designed to determine if in fact maintenance treatments were really more effective in prolonging a patient's survival than no treatments while asymptomatic followed by simple re-treatment after symptoms recurred, and (c) the fact that re-treatment only after symptoms recurred might actually be more cost-effective for patients than maintenance treatments.

35. Despite that slide's acknowledgment that "maintenance" is an off-label indication, and thus "dictate[s] lack of ability to promote," and despite the "threats" just listed, the same C & P presentation included a slide entitled "Achieving the Vision: Start a Revolution." This slide urged sales representatives to promote Rituxan by targeting both physicians and patients. With physicians the representatives' goal was to "…Persuade Belief in C&P [maintenance] Clinical Benefit ***and*** Compel to Increase use." With patients, Genentech's goal was to "…Educate, Stimulate and Inspire patients to Be in Control of Their Disease ***and*** Request C&P [maintenance]." (Emphases in original.)

36. Genentech management encouraged its sales personnel not to limit themselves to marketing Rituxan for treatment of symptomatic patients. In a February 2002 Sales and Marketing meeting in San Diego, management posed a question to sales personnel and then answered that question: "What is the Positioning you are going to communicate? -- First – Again -- Always."

37. In October 2001 a marketing survey done for Genentech urged sales efforts that would not only induce physicians to prescribe Rituxan for asymptomatic NHL patients, but would also induce them to move beyond NHL to other diagnoses: "We see Rituxan usage as a progression. Conditioning physicians to think in terms of maintenance therapy may clear the path for treating chronic ailments such as CLL [another off-label use]."

38. In January 2003, Genentech held a meeting of sales personnel to discuss "Sales Force Expectations" for 2003. This was led by Genentech's national Director of Sales and its Director of Marketing. Sales personnel were urged to "Exceed $1.3B forecast!!!" If achieved (and it was), this sales figure would represent a $300 million increase over the previous

year's sales ($1.08 billion). The sales personnel were informed that they were expected to "Establish Rituxan as the standard of care in… planned retreatment therapy [maintenance]…" as well as other off-label uses. They were told, "***Additionally,*** in 2003 we need to grow our on-label business by approximately $75M." (Emphasis added.) Thus, of the $300 million increase in sales that the sales personnel were expected to achieve, $75 million was to be on-label, and the balance, at least $225 million, would be off-label.

39. As management well knew, it was clearly impossible for sales representatives to achieve management's stated goal without off-label marketing.

40. In the same time-frame, Genentech generated a plan for using scientific publications to market Rituxan to physicians to persuade them to use Rituxan for maintenance in asymptomatic patients.

41. Under "Brand objectives in this plan," Genentech listed "Build the maintenance movement" and "Drive extended dosing." Under "Expand clinical experience," Genentech listed "Drive maintenance therapy." Under "Institutionalize Rituxan" Genentech listed "Establish belief that treating asymptomatic patients is clinically meaningful." This plan explicitly listed both doctors and patients in its "Primary audiences."

42. Genentech was well aware that the scientific community had serious doubts about the efficacy and cost-effectiveness of Rituxan for maintenance. In a presentation to its sales personnel in 2003, Susan Hopkins, Genentech's Director of Marketing, reported on a "thought leader meeting" Genentech had just sponsored in Laguna Beach, California, attended by national specialists in NHL. Ms. Hopkins told the sales representatives that one of the doctors in that thought leader meeting had asked the others a hypothetical question: "Let's say that you

are diagnosed with indolent NHL today. How many people in the room would want to be on Rituxan maintenance? One physician raised his hand. That was out of eleven."

43. Sales representatives, moreover, regularly reported to their supervisors that they were encountering resistance in the field from physicians who were reluctant to prescribe Rituxan for maintenance without the evidence provided by significant clinical trials.

44. Off-label promotion of Rituxan for maintenance was hugely profitable to Genentech, however, in part because the drug itself is extremely expensive, costing approximately $3,000 per infusion for an NHL patient. Because a typical maintenance regimen for an asymptomatic patient was four weekly courses repeated at six-month intervals for two years, each time Genentech succeeded in persuading a single doctor to put a single patient on Rituxan for maintenance, the revenue to Genentech was about 16 times $3,000, or about $48,000.

45. For a CLL patient, the cost was even higher. One of management's presentation slides entitled "Value of Maintenance Patient" estimated the cost of one infusion as almost $4,000 for a CLL patient. Estimating the cost of a "very aggressive" maintenance scenario, as Genentech did, that one patient's maintenance cost alone came to nearly $100,000 over five years.

46. Genentech was well aware that Medicare was paying for approximately 50% of the Rituxan it sold. Indeed, Genentech priced Rituxan with Medicare in mind.

47. Genentech raised its price for Rituxan in 2004, for example, not because of any economic necessity, but because its research showed that a "psychological threshold" on

the part of doctors and patients would permit an increase of up to 5%, and because it wanted to meet Genentech's own "brand targets." Genentech considered timing this price-raise so that it would not be tied too directly to an increase in Medicare reimbursement: "September timing provides some separation from CMS [Medicare and Medicaid administration] reimbursement increase." Genentech also used the news of the increase in Medicare reimbursement to soften the news of Genentech's own price increase: "September timing lets field leverage positive news of reimbursement increase."

48. Genentech and doctors had a strong incentive not to inform Medicare and other third-party payors of the off-label nature of prescriptions for which reimbursement was being requested, for the most part they did not do so. In some instances when third-party payors became aware that a claim for Rituxan reimbursement was being made for off-label maintenance, for example, the third-party payors refused to reimburse for such "non-essential" drugs, and this generated significant problems for Genentech.

49. Genentech had promised providers in writing that Genentech would help providers appeal from any refusal to reimburse for Rituxan, and if the appeal were unsuccessful, Genentech would reimburse the doctor-claimants with free doses of Rituxan (the "drug replacement" program). This obviously reduced Genentech's profits by the value of the free product.

50. Moreover, medical care providers who submitted claims for uses that were disclosed as for off-label uses had more difficulty in the claims reimbursement process, and this in turn caused resistance to off-label Rituxan sales.

51. In 2002, for instance, Mount Sinai Medical Center in New York City told Genentech that because of all the paperwork involved, all patients who wanted Rituxan for off-label uses would have to pay for it themselves. A Genentech sales representative reported in an emergency email that, "since 85% of Rituxan sales comes from off indication use, [Genentech] need[s] to make sure..." that Mount Sinai understands that Genentech has a special branch ("SPOC" or "Single Point of Contact") devoted entirely to helping medical providers with reimbursement issues, and Genentech needs also to be sure that the benefits coordinator at Mount Sinai does not adopt "any protocol that limits the use of Rituxan to only on-label use—which is what she is proposing."

52. Genentech's fear that Medicare would refuse to reimburse doctors for maintenance and other off-label uses if Medicare became aware of the off-label uses was also reflected in a July 2004 Business Review of Genentech's which listed maintenance and CLL as "at risk" in terms of Medicare reimbursement.

COUNT ONE

53. The allegations contained in paragraphs 1 through 52 are incorporated herein by reference.

54. Genentech's actions with respect to the off-label marketing of Rituxan constitute violations of the False Claims Act, 31 U.S.C. §§ 3729-32.

55. As the direct, proximate and foreseeable result of Genentech's fraudulent course of conduct, as set forth herein, Genentech caused tens of thousands of fraudulent claims

to be submitted to the Medicare and Medicaid programs for prescriptions for off-label uses of Rituxan.

COUNT TWO

56. The allegations contained in paragraphs 1 through 52 are incorporated herein by reference.

57. Another tool employed by Genentech to promote Rituxan was the practice of inviting "key" oncologists, large prescribers of Rituxan, on all-expenses-paid trips to prime vacation locations and paying them honoraria, ostensibly to advise Genentech on their experiences with Rituxan but actually to reward them for high use of Rituxan and to persuade them to continue prescribing it.

58. These so-called "Advisory Boards" were described by Genentech sales personnel as "targeted marketing" of oncologists. Genentech's sales representatives thought such "Advisory Boards" were effective in promoting Rituxan: "they build loyalty and customer dedication – Physicians feel special they are advisors." Genentech carried the cost of these meetings in its marketing budget.

59. The key Rituxan customers who were invited indeed appreciated these lavish meetings; as one doctor candidly responded to a mid-2002 Rituxan survey: "I think it's great when Genentech [sales reps] can provide information on reimbursement issues, clinical trials access to drugs, and invite us to a hell of a lot of meetings." Sales representatives also appreciated these lavish meetings; Genentech rewarded its highest-scoring sales people with an invitation to an Advisory Board meeting.

60. Genentech's repeated use of these "Advisory Boards" violates the Medicare and Medicaid Fraud and Abuse Act, 42 U.S.C. § 1320a-7b(b)(2)(B) ("the Anti-Kickback Statute"), which prohibits the offering or paying of any remuneration, directly or indirectly, in cash or in kind, to induce the recipient to purchase or recommend purchasing any good or service for which payment might be made in whole or in part under any federal healthcare program.

61. Each claim for reimbursement for any use of Rituxan, submitted to Medicare by any physician after having accepted an invitation to an "advisory board meeting," was fraudulent in that it was caused, in part at least, by Genentech's violation of the Anti-Kickback Statute.

62. As the direct, proximate and foreseeable result of Genentech's fraudulent course of conduct, as set forth herein, Genentech caused thousands of fraudulent claims to be submitted to the Medicare and Medicaid programs for Rituxan prescriptions that were ineligible for payment as a result of illegal kickbacks.

WHEREFORE, Relator John Underwood demands judgment in his favor and in favor of the United States against Defendant, as follows:

(a) judgment in favor of the United States in an amount equal to three times the amount of damages the United States has sustained because of Defendant's actions, plus a civil penalty of not less than $5,500 nor more than $11,000 for each violation of 31 U. S. C. § 3729;

(b) judgment in favor of Relator, as a Qui Tam Plaintiff, for a portion of the judgment in favor of the United States pursuant to 31 U.S.C. § 3730(d) and for all costs of this action, including, but not limited to, attorneys' fees, expert fees, and court costs; and

(c) judgment in favor of United States and Relator for such other and further relief as the Court deems just and proper.

/s/ Elizabeth K. Ainslie
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